REMARKS

Reconsideration of the above-identified application, in view of the following remarks, is respectfully requested.

Applicants thank the Examiner for discussing this matter on September 29, 2007. The telephone interview occurred between Examiner Berman and Agent. No exhibits or demonstrations were presented. The three studies as disclosed in the previously submitted Langer Declaration, the experiments disclosed in the application as filed, and the amendments as provided above were discussed during the interview.

I. Status of the Claims

Claims 1, 4–34, 94-95, and 100 - 103 are currently pending in this application and are at issue. Claims 29 – 34 are withdrawn. Claims 1, 24, 29, 30, 33, 34, 94, and 95 are amended and claim 14 is canceled herewith without prejudice. Support for the amendments to the claims for the term "biocompatible" is found at paragraphs 94 – 95 as filed and support for the bone substitute composition is found in claim 14 as filed. No new matter has been added.

II. Rejections under 35 U.S.C. 103(a)

Anseth in view of Schacht

Claims 1, 4-28, 94, 95 and 100-103 remain rejected as being unpatentable under 35 U.S.C. §103(a) over Anseth et al. (U.S. Pat. 5,902,599) in view of Schacht (U.S. Pat. 6,933,328).

The Examiner contends that Applicant's prior argument, statement of no suggestion or motivation to combine a bone substitute with the prepolymers is unpersuasive since Anseth clearly

teaches adding bone regenerating molecules into the composition in orthopedic applications (col. 8 lines 7 – 22). Anseth states:

> In orthopedic applications, bone regenerating molecules, seeding cells, and/or tissue can be incorporated into the prepolymer prior to or after polymerization or may be applied prior to or after formation of the implant at the site of implantation. For example bone morphogenic proteins such as those described in U.S. Pat. No. 5,011,691... can be used in these applications.

The currently pending claims are limited to compositions comprising a bone substitute which is an autograft, allograft, xenograft or alloplast or mixture thereof (claims 1, 24, 29, 33, and 34) or a bone substitute which is a polymer (claims 94 and 95). While Anseth states that bone regenerating molecules, seeding cells and tissue may be used, these compositions correspond to the optional bone promoting agents of the present invention (see claim 100 and para. 104-105) and not the bone substitutes. Thus, Applicants respectfully traverse. Anseth does not provide a teaching or suggestion to combine a bone substitute as defined in the present invention with a prepolymer.

The Examiner also argues that the rejection is based on employing the specific bone allografts taught by Schacht as the bone generating molecules in the compositions taught by Anseth and thus rejects the evidence as provided in the Declaration of Dr. Langer as sufficient to overcome the rejection. The Brooks study, as previously discussed, tested the samples:

LC1 – anhydrides material alone (MCPP and MSA)
LC2 – anhydrides with calcium carbonate
LC3 – anhydrides with Bioplant® HTR®
LC4 – anhydrides with calcium carbonate and Bioplant HTR®
Bioplant® HTR®
negative control

Thus, LC1 corresponds to the compositions taught by Anseth while LC3 and LC4 each contain an anhydride and a bone allograft material. The materials used in the Brooks study were Bioplant HTR® and light-hardened polymers. No redox components (i.e., chemical curing components) were used in this study (see further discussion below.).

Further, since the Brook's study involved the production of methylacrylic acid which was not neutralized, the animals were seen to develop tissue necrosis and, in some instances, died. Thus, it was determined that a curable composition of the anhydride polymers requiring 5 minutes cure time using light with no chemical curing was not an optimal bone implant material for dental purposes. (See Dr. Langer Declaration para. 29 – 30). In contrast, the presently claimed invention provides for a composition which is cured using both a biocompatible photoinitiator and a redox system. Thus, as demonstrated by the problems evident in the Brooks study, the present invention overcomes the problems with the prior art compositions and further is not obvious in view of the prior art.

The presently claimed invention teaches that by combining the anhydride with a bone substitute where the composition immediately hardens upon curing by light and redox chemistry, it and becomes load-bearing so as to provide immediate support for, i.e., installation of a crown and immediate functionality for the artificial tooth. Comparatively, compositions without the bone substitute (or with bone substitute provided as a cured ring around the neck of an implant as described by Schacht) do not provide sufficient support and rigidity in the short term (see application paragraphs [0017] and [0014]).

The Examiner has suggested an experiment demonstrating that the anhydride alone is not as useful as the anhydride with the bone substitute (i.e., HTR) would be advantageous to further prosecution. Applicants suggest that such an experiment is not necessary. The two components provide entirely different purposes, and a review of the prior experiments on both the anhydride alone (see Anseth) and a bone substitute (see references listed in Para. [0005] of the present application) in combination with the examples and experiments provided in the specification and during prosecution are sufficient to demonstrate the advantage of the present invention. The anhydride quickly degrades when used as taught in the present invention and thus is not useful for, e.g., high load-bearing bone applications (*See*, for example Anseth col. 1 line 47 and the present application at para. [0011]). While the anhydride materials alone have been shown to be a useful composition in dentistry, they undergo homogeneous, bulk degradation which is detrimental to the long-term mechanical properties of the material (see para. [0011]). In contrast, the bone substitute materials described herein are useful as an osteoconductive scaffold for newly regenerated bone (see

para. [0004]). Implanted HTR functions as a scaffold at, for example 6 months after tooth extraction and bone substitute and application of the HTR, when a crown is placed (see para. [0005]). Thus, a combination of a bone substitute and anhydride polymer allows for both the scaffolding and bone regeneration properties of the bone substitute material and the immediate functionality of the anhydride which has been cured using both light and redox chemistry.

Further, the experiment described as the Huys study demonstrates the presence of one of the secondary considerations of non-obviousness. This study, performed by Dr. Huys in conjunction with Dr. Schacht, did not provide acceptable results for the uses discussed in the present application. Failure of others remains a valid secondary considerations of non-obviousness (see Fed. Reg. 72, 57526 at 57534, citing *Graham v. John Deere Co.,* 383 U.S. 1, 17 (1966)). The fact that this study was unsuccessful in providing a viable composition is relevant to the obviousness of combining Anseth with Schacht. Further, the second in vivo study (Brooks), still did not provide the advantageous results as disclosed in the presently claimed invention. It was only when the Yukna study was performed where both photoinitiators and redox chemistry were used that the disclosed unexpected results were obtained.

The Examiner states that there is no disclosure of the kinds of initiators used in the Brooks study and states that the samples reported in the Brooks test were light cured for five minutes. Applicants state that the samples were light cured in the Brooks study as described in Dr. Langer's Declaration and noted by the Examiner. No redox initiators were used in the Brooks study. Thus, Dr. Langer's Declaration provides no disclosure of such unused redox initiators. The materials used in the Brooks study were Bioplant HTR® and light-hardened polymers and contained no redox component(s). The fact that no redox components were used in the Brooks study is evidenced by Exhibits H and I of the previously submitted Langer Declaration which discuss a light-hardened material (Exhibit H, pg. 2) that describes the tested compositions as Bioplant LC, "a new light-hardened resorbable polymer material" and does not mention any redox components added to the HTR and LC components of the material, and light cured compositions (Exhibit I pg vi, x, xiii, and xv) that were prepared "using a Optilux 4000 Light curing source for 4 [or 5] minutes" (se pg. vi, xiii, and xv). The addition of redox components was not mentioned anywhere in the

study proposal or thesis (Exhibits H and I). Further, redox components could not have been included in the samples prior to the experiments described since redox components, when combined together, will generate the initiating species for curing the admixture (see para. [0097]). Thus, each of the samples in the Brooks studies underwent light curing but not chemical curing.

The Yukna study (Example 48 of US 2006/0052471) demonstrates the unexpected results of the present invention and shows that there is significant improvement when both a photoinitiator and redox initiators are used.

The Examiner states the claims are not commensurate in scope with the showing provided. In particular, the Examiner lists the following considerations:

(1) "There is no data provided wherein the prepolymer is MCPP alone"

(2) "There is no data provided for bone substitutes other than a biocompatible microporous layered polymeric composite"

(3) "There is no data provided for photoinitiators that are not biocompatible"

(4) "There is no data provided wherein the formulation contains an oxidizing agent," and "there is no data wherein the formulation contains one of the reducing agents disclosed in the instant application"

(5) "the instant claims do not recite a porogen."

In response, Applicants have the following comments and/or arguments:

(1) Applicants respectfully state that such data is not necessary (and also not particularly valuable) for the patentability of the present invention. A composition having a prepolymer which is MCPP alone is outside the scope of the claimed invention which requires both a monomer or oligomer of a diacid or multifunctional acid and a carboxylic acid molecule which includes a crosslinkable group. Thus, an experiment where the prepolymer is MCPP alone would provide only an addition control experiment. In each of the Huys, Brooks, and Yukna studies, a number of control experiments were provided. Data from the control experiments used in these studies provided the ability to compare

the properties of the compositions of the presently claimed invention and determine experiment success. Thus, an additional control study using of MCPP in rabbits or sheep is not necessary.

(2) The claims of the present invention have been amended to recite that the bone substitute is an autograft, allograft, xenograft, alloplast, or mixture thereof (see original claim 14). Thus, the claim scope is commensurate with the examples provided.

(3) The claims of the present invention have been amended to recite that the photoinitiator is a biocompatible initiator (see paragraphs 94 – 95). Thus, the claim scope is commensurate with the examples provided.

(4) The Yukna study provided an animal model for the claimed composition having both photoinitiators and redox initiators. As shown in Example 48 of US 2006/0052471, the photo-initiators camphorquinone and ethyl-4-dimethylaminobenzoate were used along with the redox initiators from Components A and B as described previously. (Example 48 states that "4 different samples were prepared as described above" (para. [0374]). The compositions for these four samples are listed in the example (F1, F2, F3, and F4). The "as described above" refers to the previous example, Example 47, where the polymers and bone substitutes were prepared as described in Example 33 and the initiator components A and B as described in Example 28 were used. While Example 47 states that no photo-initiators were used, the initiators of Example 48 include the photoinitiators camphorquinone and ethyl-4-dimethylaminobenzoate, as described in Example 27, para. [0374]). The redox initiators used in Example 48 were benzoyl peroxide and N,N-dimethyl-p-toluidine (DMPT) (i.e., Components A and B as described in both Examples 27 and 28 (para. 314-319)). Benzoyl peroxide is an oxidizing agent and is described as a preferred oxidizing agent in paragraph [0098] of the specification. DMPT is a reducing agent, and is described as a preferred reducing agent in paragraph [0099] of the specification. Thus, the formulations used in the study as discussed in the Declaration by Dr. Langer contain both the preferred oxidizing agent and reducing agent of the present invention.

(5) Claim 1 as presently pending does not require a porogen. The Examiner has suggested that an experiment demonstrating that the composition of the present invention without the addition of a porogen as suggested at para. [0106] – 0108] would be advantageous to further prosecution.

Applicants contend that a porogen, while envisioned in a preferred embodiment of the present invention, does not define the scope of the present invention. The present invention is limited to novel compositions comprising a curable admixture of a bone substitute and a crosslinkable prepolymer, a photoinitiator, and redox component(s). As provided in the Yukna pilot study, the F4 formulation does not use a porogen whereas the F3 formulation does. This initial study demonstrated that the compositions of the present invention, either with or without a porogen, can be used advantageously to, for example, promote bone growth and/or stabilize a dental implant.

The Examiner also states that "it is not absolutely clear that it is the initiators that are the significant factors" for the unexpected usefulness of the invention. However, applicants state that absolute clarity of the mechanism of action for an invention is not the test for patentability. In fact, "[i]t is not a requirement of patentability that an inventor correctly set forth or even know, how or why the invention works." (*In re Cortright* 165 F.3d 1353 (Fed. Cir. 1999) *citing Newman v. Quigg* 877 F.2d 1575 (Fed. Cir. 1989). Thus, absolute clarity concerning why the invention works is not required. As stated by Dr. Langer, "the combination of a polymer and bone substitute as claimed in the '442 application provides a viable bone implant material which promotes regeneration of new bone, little to no inflammation and is load bearing" (see Langer Declaration, para. 38).

Thus, it would not have been obvious for one of ordinary skill in the art at the time of the invention to employ the bone allograft as taught by Schacht in combination with the crosslinkable anhydride prepolymers disclosed by Anseth. The motivations as listed by the Examiner and discussed herein are not sufficient to provide the invention as claimed. At the time of the invention, Schacht did not contemplate, and had no reason to contemplate, combining a bone substitute with the prepolymers of Anseth and further to use both light and redox chemistry to cure the composition.

Thus, the present claims are not obvious, and applicants respectfully request that the rejections be withdrawn.

III. Conclusion

In view of the above amendments and remarks, applicants believe that each of the pending claims in this application is in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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